

April 15, 1969

Dr. Paul Kotin
P.O.Box 12233
Research Triangle Park, North Carolina

Dear Dr. Kotin,

I have been trying to reach you by phone today but it maybe just as well if I can get this letter to you before talking to you over the wire.

The question I want to raise with you concerns the biological effects of Chloramine and its derivatives as are abundantly produced in water supplies subjected to residual chlorination. There is, of course, an enormous literature on the bactericidal efficacy of these procedures but I have been able to ~~find essentially~~ find no information concerning the possible impact on human health of chronic uptake of these materials. The problem is obviously enormously compounded by the very wide range of substances with which chloramine is expected to react in natural waters supplies. It undoubtedly will become greatly exacerbated as the pressures on available water call for the use of more and more chlorine for its decontamination.

The specific issue in which I am most deeply interested myself concerns the possible ~~immunogenic~~ ^{mutagenic} effect of such materials. I was startled to find that amino acids and peptides as well as the nitrogenous bases of nucleic acids all react readily with chlorine to form chloramines of varying degrees of stability and further reactivity. I had, in fact, given some small thought to this kind of issue many years ago and gone so far as to test iodine with a rather negative result. However, I was not then aware of the prevalence of semi-stable complexes of chlorine which could serve to carry this chemical reactivity far more deeply into tissues and cells than would be possible for the much more highly reactive free halogen.

I have also been startled to be unable to find any convincing literature on the mechanism of action of chlorine as a bactericidal agent and on rather general grounds would give priority of place to the likelihood that its target is in fact DNA as is the case for ionizing radiation and for a range of other toxic chemicals. The capacity of chlorine to inactivate a range of viruses is consistent with this view, although it is, of course, impossible without specific experiments to disentangle the role of proteins versus nucleic acids as the target molecules.

I am in the course of starting some experiments on this question. But I would be most grateful for on your part any further assistance in scouring the literature for relevant publications which I have been notably unsuccessful in finding for myself. What I have particularly in mind are cellular toxicity tests of various forms of chlorine complexes, specific evidence of reactions with well-defined target molecules, and in particular any explicit test of the possibility of the production of genetic damage.

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I have also been unable to find any significant work on the transport of chlorine from chlorination procedures into the animal or human body which would, of course, be most relevant to any practical concerns about the entire matter.

You will correctly suspect that I also have in mind sensitizing you to the public policy implications of this speculation but I would, of course, hasten back to the laboratory to find out whether there is real substance to that.

Sincerely yours,

Joshua Lederberg
Professor of Genetics

JL/rr